CLINICAL VIGNETTE

Subacute Cutaneous Lupus Erythematosus Induced by Palbociclib

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Case Summary

A 67-year-old female with past history of stage IIA right breast cancer diagnosed twelve years ago, presented with loco-regional recurrence in the right axilla and bone metastases. Lymph node biopsy revealed recurrent invasive ductal carcinoma, consistent with prior diagnosis, estrogen receptor 90% positive, progesterone receptor 60% positive, and HER2-neu receptor negative. She was initiated on systemic therapy with letrozole and palbociclib. Within 1 month of starting therapy, her right upper extremity numbness and tingling and right axillary pressure resolved. Within 6 months, she had no evidence of FDG avid disease on PET-CT. Approximately 3 months after starting treatment she noted a new erythematous, mildly pruritic rash on her anterior chest. Initial trial of hydrocortisone 1% cream was not beneficial. The skin papules coalesced and became annular and polycyclic. They were particularly severe over the anterior neck and upper back. She was seen by her dermatologist who prescribed various topicals including crisabrole 2%, flucandrenolide 0.05%, and tacrolimus 0.1% and 0.5%, all of which were ineffective and caused further skin irritation. She eventually underwent skin biopsy of the right upper back, which showed superficial and deep perivascular and lichenoid chronic dermatitis with increased interstitial mucin, subepidermal basement membrane thickening, and necrotic basilar epidermal keratinocytes. These histologic findings were most suggestive of subacute cutaneous lupus erythematosus (SCLE). No evidence of metastatic breast cancer was noted on skin biopsy. Subsequent labs were remarkable for positive +ANA at 1:160 homogenous pattern, as well as elevated SSA and SSB at 89 and 61, respectively. Antihistone histone antibody was negative. Rheumatology did not feel there was evidence for active systemic lupus erythematosus. Given the time course, a diagnosis of drug induced SCLE (DI-SCLE) by palbociclib was favored. She was started on hydroxychloroquine 400mg daily and within 2 weeks, her rash had resolved.

Discussion

DI-SCLE was first described in 1985, with an increasing number of drugs associated with its development. DI-SCLE may be clinically indistinguishable from idiopathic SCLE clinically, histopathological and immunologically, however the diagnosis is favored if it occurs following initiation of a drug along with resolution following drug cessation. These include antiarrhythmics, antifungals, antineoplastics, beta blockers, calcium channel blockers, diuretics, non-steroidal anti-inflammatories, and others.[2] In addition, numerous case reports of aromatase inhibitor induced autoimmune disorders including SCLE have been reported. In a case-control study of 234 patients in Sweden with SCLE, approximately one-third of cases were related to drug exposure.[2] It generally presents with the typical photosensitive symmetric, nonscarring annular polycyclic, or papulosquamous lesions, and has more limited skin lesions than idiopathic SCLE.[3] Systemic involvement is rare.

In a systematic review of DI-SCLE most patients affected by drug-induced SCLE female (72%) with a mean age of 58 years. The immunological profile includes frequent presence of anti-Ro/SSA and/or anti-La/SSB, together with ANA and anti-histone antibodies. Anti-Ro/SS-A is equally prevalent in drug-induced and idiopathic SCLE. The majority of patients who are Ro/SS-A or La/SS-B positive do not become negative after disease resolution. Anti-histone antibodies are positive in one-third of the cases.[4] This immunologic profile is consistent with what is seen in our patient.

Palbociclib is a cyclin dependent kinase (CDK) 4/6 inhibitor approved for first line use in combination with letrozole in metastatic breast cancer. It has been reported in only one prior case of SCLE.[5] The landmark PALOMA-2 trial, which led to approval, demonstrated a significant improvement in progression free survival (PFS) from 14.5 months with letrozole alone to 24.8 months with the addition of palbociclib in post-menopausal women.[6] Common adverse reactions, observed in 10% or more of patients taking palbociclib were neutropenia, infections, leukopenia, fatigue, nausea, alopecia, stomatitis, diarrhea, anemia, rash, asthenia, thrombocytopenia, vomiting, decreased appetite, dry skin, pyrexia, and dysgeusia. The most frequently reported grade 3 or greater adverse reactions in patients receiving palbociclib plus letrozole were neutropenia, leukopenia, infections, and anemia.[6] In addition to palbociclib, two other CDK 4/6 inhibitors are approved for use in the metastatic setting, ribociclib and abemaciclib. They are now being widely studied in the neoadjuvant and adjuvant settings.

Treatment for DI-SCLE consists of discontinuation of the drug. For severe or refractory cases systemic corticosteroids may be used. Some patients may need additional immunosuppressive therapy, including azathioprine, cyclophosphamide, methotrexate, hydroxychloroquine or mycophenolate. Our patient's breast cancer was well controlled with letrozole and palbociclib, prompting the decision not to discontinue palbociclib.

She declined steroids and was started on hydroxychloroquine. Although there are more reports of aromatase inhibitors causing DI-SCLE, as the patient previously tolerated aromasin, a steroidal aromatase inhibitor, for 5 years without similar incident, the more likely culprit is palbociclib. She continues on hydroxychloroquine without recurrence of her rash.

With an increasing use of CDK 4/6 inhibitors in advanced breast cancer and potential for use in early stage disease, it is important for clinicians to be aware of this rare but possible side effect so that it may be managed promptly and appropriately.

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